PAEDIATRIC GASTRO-OESOPHAGEAL REFLUX DISEASE (GERD) – A RELOOK AT A COMMON PROBLEM

Marion Aw

Recurrent vomiting is common in infants. Whilst the majority of children have uncomplicated gastro-oesophageal reflux (GER), a careful assessment of the history and physical examination is necessary in order to detect the minority of patients who would require further evaluation and specialist referral. An awareness of the variety of clinical features and associations of GERD and an understanding of the strengths and weakness of diagnostic tests currently available would enable clinicians to choose the most appropriate ones for evaluating individual patients. This would help in clarifying diagnosis and eventual improved patient care.

Contents
- Definition
- Typical and atypical manifestations
- Evaluation & Diagnostic Investigations
- Common clinical associations of GERD
- Treatment options
- Algorithms for management
Definition

Gastro-oesophageal reflux (GER) is defined as the passage of gastric contents into the lower oesophagus. It is a physiologic occurrence in healthy individuals (infants, children and adults) throughout the day. In the majority of instances episodes of reflux are brief and do not extend above the lower oesophagus.

GER is particularly common in infancy and manifests most frequently as episodes of regurgitation or vomiting. It the vast majority GER is harmless, self-limiting and can be viewed as a physiological variant rather than a disease. In a community survey of 948 infants, 50% of infants vomited at least once per day in the first 3 months of life. This figure was as high as 67% of four-month-old infants, and decreased to 21% by 7-9 months. However, by the age of 12 months, 5% of infants were still vomiting at least once /day.

![Bar chart showing vomiting frequency by age group](image)

Gastro-oesophageal reflux disease (GERD) is said to occur when this passage of gastric contents into the oesophagus or oropharynx produces complications. The symptoms of GERD are protean. Infants can present with anorexia, arching, irritability, anaemia, haematemesis or failure to thrive. It is also recognised as one of the causes of acute life-threatening events (ALTEs) as well as chronic respiratory disorders such as persistent stridor, wheeze and recurrent pneumonia. In older children and adolescents, GER is more likely to manifest adult-type pattern of chronic heartburn. (Table 1)

GER has also been increasing recognised as a cause of upper airway symptoms such as hoarseness, chronic cough and globus sensation. These symptoms usually occur in the absence of classical symptoms of GER such as regurgitation, heartburn or chest pain. It has also been linked to otalgia, otitis media with effusion (glue ear) and recurrent rhinopharyngitis. Children with GER have also been shown to have an increased prevalence of tooth erosion and dental caries.
Table 1. Typical and Atypical symptoms of GERD

<table>
<thead>
<tr>
<th>Typical</th>
<th>Atypical</th>
</tr>
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<tbody>
<tr>
<td>Vomiting</td>
<td>Hoarseness</td>
</tr>
<tr>
<td>Nausea</td>
<td>Pharyngeal dryness</td>
</tr>
<tr>
<td>Heartburn</td>
<td>Sore throat</td>
</tr>
<tr>
<td>Acid taste</td>
<td>Excessive salvation</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Neck Pains</td>
</tr>
</tbody>
</table>

Diagnostic Evaluation of a child with suspected GERD

Numerous disorders can present with recurrent vomiting and the diagnostic challenge is to be able to distinguish between vomiting due to GER and vomiting secondary to these other conditions. (Table 2) In most instances a thorough history and physical examination would be sufficient to determine if the diagnosis is uncomplicated GER. In the absence of warning signs and symptoms, diagnostic tests are generally not required (Table 3).

Table 2. Differential Diagnosis of recurrent vomiting

<table>
<thead>
<tr>
<th>Gastrointestinal Obstruction/Disorders</th>
<th>Pyloric stenosis</th>
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<tbody>
<tr>
<td></td>
<td>Antral/duodenal web</td>
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<tr>
<td></td>
<td>Malrotation/intermittent volvulus</td>
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<td></td>
<td>Intestinal duplication</td>
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<tr>
<td></td>
<td>Gastroesophageal Reflux</td>
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<tr>
<td></td>
<td>Food allergy/intolerance</td>
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<tr>
<td></td>
<td>Eosinophilic oesophagitis</td>
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<tr>
<td>Neurologic/Raised intracranial pressure</td>
<td>Hydrocephalus</td>
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<tr>
<td></td>
<td>Subdural haematoma</td>
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<tr>
<td></td>
<td>Intracranial tumours</td>
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<tr>
<td></td>
<td>Meningitis</td>
</tr>
<tr>
<td>Infection</td>
<td>Urinary tract infection</td>
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<tr>
<td></td>
<td>Sepsis</td>
</tr>
<tr>
<td></td>
<td>Otitis Media</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Urea cycle defects</td>
</tr>
<tr>
<td></td>
<td>Amino or Organic acidaemias</td>
</tr>
<tr>
<td></td>
<td>Congenital adrenal hyperplasia</td>
</tr>
</tbody>
</table>
Table 3. Warning symptoms and signs

<table>
<thead>
<tr>
<th>History</th>
<th>Onset after 6 months of age</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Forceful vomiting</td>
</tr>
<tr>
<td></td>
<td>Bilious vomiting</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal bleeding</td>
</tr>
<tr>
<td></td>
<td>(haemetemesis/haematochezia)</td>
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<tr>
<td></td>
<td>Diarrhoea/constipation</td>
</tr>
<tr>
<td></td>
<td>Fever/Lethargy</td>
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<tr>
<td></td>
<td>Poor weight gain</td>
</tr>
<tr>
<td></td>
<td>Seizures</td>
</tr>
<tr>
<td>Signs</td>
<td>Unwell child</td>
</tr>
<tr>
<td></td>
<td>Macro/microcephaly</td>
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<tr>
<td></td>
<td>Full fontanelle</td>
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<tr>
<td></td>
<td>Hepatosplenomegaly</td>
</tr>
<tr>
<td></td>
<td>Abdominal distension/tenderness</td>
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<tr>
<td></td>
<td>Associated genetic/syndromic disorders</td>
</tr>
</tbody>
</table>

Where necessary, the aims of diagnostic tests would be to:

1. Document the presence of GER
2. Detect the presence of complications such as oesophagitis
3. Establish a causal relationship between GER and symptoms
4. Evaluate therapy
5. Exclude other causes of symptoms

**Oesophageal pH monitoring**

Oesophageal pH monitoring is recognised at the ‘gold standard’ test for the detection of oesophageal acid exposure. The test utilizes a microelectrode placed trans-nasally into the lower oesophagus to measure and record lower oesophageal acid exposure over a period of time. Computerised analysis can then be used to calculate the number and duration of reflux episodes. The percentage of total time that the lower oesophageal pH is < 4 is called the reflux index. It is considered the most valid measure of reflux because it reflects the cumulative acid exposure of the lower oesophagus. Oesophageal pH monitoring can also be used to determine if there is a temporal association between acid reflux and the patient’s symptoms and to assess the adequacy of therapy in patients receiving acid suppression therapy.

The major drawback of pH monitoring is that it does not detect non-acid reflux episodes. The other important point to note is that oesophageal pH monitoring may be normal in some patients with GERD, and therefore a negative test does not exclude its presence.
Barium Contrast Study

The main aim of the barium contrast studies is to detect structural abnormalities of the upper gastrointestinal tract, such as pyloric stenosis, annular pancreas, oesophageal webs/stenosis, malrotation and hiatal hernia that may be the underlying pathology causing the patient’s symptoms. It is neither sensitive nor specific for the diagnosis of GER per se. Its brief duration can result in false negative conclusions, whilst the frequent occurrence of non-pathological reflux may result in a high false positive rate.

Endoscopy and Biopsy

Upper gastrointestinal (GI) endoscopy is useful in assessing the presence and severity of oesophagitis, strictures and Barrett’s oesophagus in patients who present with typical symptoms. At the same time it can be used to exclude other disorders such as eosinophilic oesophagitis, infectious oesophagitis and Crohn’s disease in children who present with recurrent vomiting, chest and/or abdominal pain. A normal appearance of the oesophagus during endoscopy does not exclude histopathological oesophagitis, and biopsy is recommended when endoscopy is performed to detect microscopic oesophagitis and to exclude causes of oesophagitis other than reflux.

Studies have shown that the presence of endoscopic and histopathological oesophagitis is strongly correlated with abnormal oesophageal pH monitoring. In children with endoscopic oesophagitis (ulcerations or erosions) or biopsy proven oesophagitis, approximately 95% will have an abnormal reflux index. However, the converse is not necessarily true. Endoscopic oesophagitis was present in only 50% of patients with positive oesophageal pH monitoring. In addition, the severity of the oesophagitis does not correlate with the reflux index.

Scintigraphy

A nuclear scintiscan is performed by the oral ingestion or instillation of technetium-labelled formula or food. The stomach, oesophagus and lungs are then scanned for evidence of GER and aspiration. The advantage of the nuclear scan is that it can demonstrate reflux of non-acid gastric contents. In addition, if episodes of aspiration are not detected during the study period, repeat imaging can be obtained up to 24 hours after the feed is administered to detect any presence of radioactivity in the lungs. Similarly to pH monitoring, a negative scintiscan does not exclude the possibility of infrequently occurring aspiration.

Electrical Impedance

There has been recent interest in the use of electrical impedance studies to detect GER. This method utilises the detection of changes in electrical impedance in the body of the oesophagus with the passage of a food or fluid bolus. It is a pH-independent technique and data can be analyzed for bolus composition, reflux height, duration, and clearance.
As it is pH-independent, it may prove to be a more sensitive diagnostic tool to detect GER in infants fed mainly alkali containing milk compared to conventional oesophageal pH monitoring.

**Colour Doppler**

Ultrasound examination has also been used to detect the backward flow of gastric contents into the oesophagus in children. A study in infants < 1 year with recurrent vomiting showed fairly good correlation between Doppler studies and pH recording. Advantages with ultrasound include its non-invasive nature and the fact that it can detect any episode of reflux regardless of pH. Its disadvantages are that it looks only at a brief window of time, and it may be difficult to quantitate or correlate reflux with events like coughing and asthma.

**Common Clinical Scenarios associated with GER/GERD**

**Uncomplicated GER**

The classic case scenario of a “happy spitter” is a well-looking infant who presents with effortless painless vomiting and otherwise normal growth parameters. Most would outgrow the problem and need no or very little intervention besides parental reassurance and education. There is no evidence that pharmacological therapy affects the natural history of uncomplicated GER in infants.

If symptoms worsen or do not improve by 18-24 months, then further evaluation could be considered (as below).

**Cow’s milk protein allergy**

It has been recognised that some infants with GER symptoms may have underlying cow’s milk protein allergy (CMA). In reported studies, the prevalence of CMA in infants evaluated for GER was between 20- 30%. Often, CMA may be clinically indistinguishable based on history and physical examination alone. In these instances a 2-week trial of hypoallergenic formula has been recommended.

**Child over 2 years with recurrent regurgitation or vomiting**

Some children still have episodes of regurgitation/vomiting at the age of 2 years. They usually vomit between once a day and once a week. It is neither bilious or bloody and not associated with pain or discomfort. It often occurs post-prandially or with exertion. There are no published studies describing the best management of these children, and current recommendations are an upper gastrointestinal series to exclude an anatomic abnormality with or without endoscopy and biopsy. A therapeutic trial of pharmacologic treatment may be considered at this point, and continued for a period if there is good therapeutic response.
Infant with recurrent vomiting and poor weight gain

In this scenario, a good dietary history to assess adequacy of calories offered and ingested by the infant is essential. Questions on the way formula is prepared (or diluted), how it is being fed to the infant and the presence of pain or difficulty associated with feeding are important. Assessing mother-infant interactions and exploring family dynamics may identify potential stresses that may explain the infant’s poor weight gain. A condition termed “nervous vomiting” results from poor maternal-infant interaction, leading to irritability, vomiting, feeding difficulties and failure to thrive in the infant. Maternal anxiety has been shown to cause increased muscle tension, which is transmitted to the infant, as evidenced by increased muscle tone and heart rate. It has been recognised that aberrations in normal infant-caregiver relationships can lead to visceral reactions manifested by GER, pylorospasm or failure to thrive.

If the infant is still failing to gain weight despite ingestion of adequate calories, further diagnostic tests need to be performed. Investigations include full blood count, urea/electrolytes, liver function tests, urinalysis, metabolic screen, barium studies, endoscopy with biopsy, and if necessary a period of observation in hospital.

Infant with irritability/feeding refusal

There are very few paediatric studies evaluating the association of oesophageal pain causing irritability, feed refusal or sleep difficulties. In one study, simultaneous video and oesophageal pH monitoring showed an association between grimacing and reflux episodes. However another showed no correlation between excessive crying and oesophagitis. With regards to feeding difficulties, the causal association in infants is even less clear. Although some case series have described feeding difficulties as potential symptoms of GER, none have demonstrated that GER is causally related to the feeding difficulties or that feeding improves following treatment. Because a large number of disorders may contribute to infant feeding difficulties, empiric therapy for GER is generally not recommended for this group of infants.

Child with Heart burn/chest pain/dysphagia

Retrosternal chest pain, regurgitation of sour taste in the mouth, odynophagia (pain during swallowing) and dysphagia (difficulty in swallowing) are recognised symptoms of reflux oesophagitis. There are no randomised placebo controlled trials of treatment conducted in children/adolescents in this age group, and results have been postulated from adult experience. Measures include lifestyle changes, the avoidance of known precipitating factors (such as caffeine, alcohol, chocolate and spicy foods and smoking) and a 2-week trial of H2 Receptor Antagonists or Proton Pump Inhibitors. If no improvement occurs then the patient should be evaluated with upper GI endoscopy and biopsy.
In children with dysphagia and odynopahgia, a barium study should be considered at the least, with/ without endoscopy to exclude an anatomic abnormality, motility disorders or oesophagitis as the cause of the symptoms.

**Infant with Apnoea or ALTE**

In infants with acute life threatening events (ALTEs), the prevalence of recurrent regurgitation and vomiting has been noted to be as high as 60-70%, with 40-80% having abnormal oesophageal pH monitoring. However a temporal association between episodes of GER and apnoea/bradycardia may not often be demonstrated, and several studies also note that many infants had episodes of apnoea unrelated to episodes of GER, suggesting a primary impairment of the regulation of respiration. At the same time, in a follow-up period over 2 months, the co-existence of GER in infants with ALTE did not predict the risk for subsequent episodes of prolonged apnoea or bradycardia.

The closest evidence for a possible causal association between ALTE and GER, and therefore infants who are more likely to respond to anti-reflux therapy are those in whom there is gross emesis or oral regurgitation at the time of the ALTE, when the episodes occur in the awake infant, and when the ALTE is characterised by obstructive apnoea.

**Infant/Child with Asthma or Chronic respiratory complaints**

GER is regarded as the third most frequent cause of chronic cough after asthma and chronic sino-bronchial syndrome. In reported studies, as many as 60-75% of children with asthma, poorly responsive to conventional treatment had abnormal pH monitoring studies. In addition, it has also been recognised that these children may have GER in the absence of classic reflux symptoms.

It is a never-ending debate whether asthma in these patients is the result of reflux or vice versa. Most likely, it is a dynamic inter-relationship, where reflux aggravates the course of asthma, and asthma in turn enhances the reflux. Although this causal relationship between asthma and GER remains unclear, there is evidence that some patients experience marked improvement after pharmacologic treatment of GER.

GER should be suspected as the cause or contributory factor for asthmatic symptoms in patients with

1. Asthma and either typical or atypical symptoms of GERD
2. Asthma and a negative family history, no signs of atopy, signs of treatment resistant asthma, or aggravation of symptoms after theophylline

Patients with persistent asthma who fail to respond to standard asthma therapy and in whom classic symptoms of GERD exist, a trial of vigorous, prolonged medical therapy
of GER is recommended. In those without symptoms of GER, oesophageal pH monitoring would be indicated.

**Child with Recurrent Pneumonia**

The incidence of GER–related recurrent aspiration in normal infants and children is unknown, but appears to be rare. Some patient populations are prone to aspiration. The presence of neuromuscular disease or a history of laryngeal or oesophageal anatomic abnormalities increases the risk of aspiration during swallowing following episodes of reflux. Unfortunately, in these cases, a normal pH study does not exclude GER as a cause of aspiration pneumonia and other tests would need to be performed. These include evaluation of airway protective mechanisms, videofluoroscopy, bronchoscopy and lavage for lipid-laden macrophages and nuclear scintigraphy.

In these specific groups of patients, treatment decisions are made taking into account the morbidity of recurrent episodes of aspiration and deterioration to lung function on the one hand, against the risks and benefits of surgical therapy on the other. Unfortunately, there are no controlled studies evaluating the benefit of medical or surgical options in preventing chronic lung disease caused by GER in children.

**Management of GERD**

The approach to the management of GER is age and symptom dependent. Treatment where necessary would include one or more of the following three:

1. **Lifestyle changes**
   - Infants: alterations in formula composition or sleep positioning
   - Adolescents: dietary modifications, weight reduction

2. **Pharmacologic therapy** (Table 4)
   - Acid suppression therapy
   - Prokinetic agents

3. **Surgery**
   - Open or laparoscopic fundoplication

**Table 4: Pharmacological Therapy for GERD**

<table>
<thead>
<tr>
<th>Action</th>
<th>Recommended oral dose (adult max)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acid Suppression</strong></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td>40 mg/kg/day tds/qds</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>4-8 mg/kg/day bd</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>1 mg/kg/day bd</td>
</tr>
<tr>
<td></td>
<td>3.5 mg/kg/day</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>0.73-1.6 mg/kg/day</td>
</tr>
<tr>
<td><strong>Prokinetic</strong></td>
<td></td>
</tr>
<tr>
<td>Domperidone</td>
<td>0.2-0.4 mg/kg/dose tds/qds</td>
</tr>
<tr>
<td>Cisapride**</td>
<td>0.2 mg/kg/dose tds/qds</td>
</tr>
</tbody>
</table>
*References for drug doses:

**Used only on a named patient basis. Not to be used in patients with cardiac, liver or electrolyte abnormalities. (FDA recommendations: ECG, K++, Ca++, Mg++ and creatinine before administration)

**Medical Management of GERD**

Medical management includes a combination of modifications to feeding and positioning with or without pharmacological therapy. Milk-thickening agents have been shown to decrease the number of episodes of reflux, but do not improve symptom scores per se. The use of cereals to thicken milk feeds may have the added advantage of increasing the calorie density of feeds. Other techniques include the frequent small bolus feeding, overnight naso-gastric tube feeding and naso-jejunal feeding. However, there are no studies comparing the efficacy of these approaches with pharmacological and/or surgical therapy.

Prone positioning is one of the most powerful anti-reflux therapies for young infants, reducing acid reflux by 80% compared with either supine or lateral recumbent positions. However, concerns about SIDS have reduced the use of this therapy. Current recommendations are for supine position unless in exceptional cases where the risks of aspiration as a complication of GERD far out-weigh the risk of SIDS. The American Academy of Pediatrics guidelines for infants < 12 months are that supine positioning confers the lowest risk for SIDS and is preferred. Prone positioning as anti-reflux therapy is acceptable while the infant is awake, particularly in the postprandial period.

**Surgical Treatment for GERD**

Surgery is indicated for children with chronic GERD and persistent complications despite medical therapy. The Nissen fundoplication is the most common surgical procedure. With advances in surgical technique, laparoscopic fundoplication has been gaining wider acceptance, and being performed in favour of the open technique if there are no surgical contraindications.

Following fundoplication, complete resolution of symptoms varies from 60-90%. The most commonly described specific complications include breakdown of wrap, bowel obstruction (oesophageal/small bowel), gas bloat syndrome and wound infection. Re-operation rates are between 3-18.9%.
Suggested Management Algorithms

**Recurrent vomiting**

History and physical exam

Are there warning signals or signs of complicated GERD?

Yes → Evaluate further

No

Uncomplicated infantile GER “Happy spitter”

Resolves by 18 to 24 months of age?

Yes → Well child

No

1. Parental education
2. Tests usually not necessary
3. Consider
   - Thickened formula
   - Hypoallergenic formula

1. Paediatric GI referral
2. Evaluate need for investigations:
   - Barium study
   - OGD + biopsy
   - Oesophageal pH monitoring
   - Acid suppression +/- or prokinetic
Vomiting and FTT

History and physical exam

Are there warning symptoms or signs?

Yes → Consider other diagnosis

No

Are adequate calories given/consumed?

Yes

No → Education/Dietitian referral Follow-up closely

Investigations to consider:
1. FBC
2. Urea / Electrolytes
3. Barium study
4. Assess swallowing
5. Lactate/metabolic screen

Abnormal?

Yes → Manage accordingly

No

1. Paediatric GI referral
   Specialised investigations eg. OGD + biopsy
2. Hospitalize
   • Optimize medical therapy
   • Observe parent-child interaction
   • Consider NG or NJ tube feeding
Chronic Heartburn

History and physical exam

Education
Lifestyle changes
PPI/H₂RA x 2-4 weeks

Resolves

Yes
Stop Medication

No

Paediatric GI referral
OGD + biopsy

Yes
Relapse soon?

No
Observation
Persistent Asthma

History and physical exam

Heartburn reflux symptoms

Yes

High dose H$_2$RA or PPI

No

Consider need for pH monitoring

Yes

Improvement in asthma

Discontinue medications Observe

No

Normal

Repeat pH study Optimise treatment Prokinetic / Fundoplication

No GER treatment

Optimise treatment Prokinetic / Fundoplication

No